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EXAMINER MORAN, MARJORIE A				
ART UNIT			PAPER NUMBER	
1631				

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/026,110

Applicant(s)

CHENG, JILL

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,7,13-15 and 46-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7,13-15 and 46-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                                  |                                                                                         |
|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                      | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                             | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>8/11/06</u> . | 6) <input type="checkbox"/> Other: _____                                                |

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/11/06 has been entered.

Claims 1, 7, 13-15, and 46-51 are pending. All rejections and objections not reiterated below are hereby withdrawn.

***Information Disclosure Statement***

The IDS filed 8/11/06 has been considered in full.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 7, 13-15 and 46-51 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to methods for analyzing gene expression comprising only steps of mathematical manipulation. Neither of the claimed methods recites a physical transformation of matter. In the absence of a physical transformation of matter, method (process) claims may be statutory where they recite a concrete, tangible and

useful result. The final step of claim 1 is one of performing statistical methods while the final step of claim 46 is one of clustering. None of the claims recites an actual, concrete result nor does any claim recite outputting or otherwise communicating a result to a user in tangible form. Thus, the claims fail to recite a result which is concrete, tangible and useful. As the claims recite neither a physical transformation of matter nor a concrete, tangible and useful result, they are not statutory.

Applicant is invited to review the most recent Guidelines with respect to statutory subject matter, which were published in an OG Notice on 22 November 2005.

Applicant's arguments filed 8/11/06 have been fully considered but they are not persuasive. In response to the argument that the claims recite manipulation of data "representing physical objects," it is noted that data manipulation is not a *physical* transformation of matter. In response to the argument that data is "transformed" into computer data by pre-compute process activity, it is noted that none of the claims recites steps of entering data or performing other "pre-computer" acts. The first step of "obtaining data" may, in fact, be performed by the computer (e.g. by retrieving data from a previously existing file) and is not limited to be either a physical act nor one performed outside the computer. Further, even if "obtaining data" were to be interpreted as "entering data", which it is not, merely entering data into a computer does not transform either the data itself nor the computer itself into another state or thing, and therefore is not a physical transformation of matter. The data remains the same whether it is written on paper or exists electronically in computer memory. For these reasons and those set

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forth above, the examiner maintains that the claims do not recite statutory subject matter.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> para***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, and 13-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A method of analyzing gene expression comprising “performing one or more statistical methods” to grouped expression levels, as recited in amended claim 1, is new matter. Applicant does not point to support for any of the claim amendments in the response filed 8/11/06. The originally filed specification discloses, on pages 2 and 19-20, analysis of grouped or clustered data. A disclosure for “analysis” is not supportive of “performing one or more statistical methods.” The instant specification does not, in fact, disclose “statistical methods” anywhere nor does it disclose any particular “statistical” analysis. Original claim 1 recited “analysis” which was further limited in original claims 4-6 to be clustering or data mining. None of the original claims recited “statistical methods” nor “statistical” analysis. As the originally filed disclosure does not

provide support for the newly recited limitation of claim 1, the claims recite new matter and are rejected.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> para***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 13-15 and 46-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 46 recite the phrase “database ...being designed” in lines 6 and 7, respectively. It is unclear whether applicant intends a method step (design of a database) or a “product by process” limitation (one which comprise information resulting from a design step) or merely intends to limit the database to comprise particular kinds of information/data. As it is unclear what limitation is intended, the claims are indefinite. If a method step is intended, then this rejection may be overcome by reciting the step in active, positive language, and by delineating the step with a separate indent. If a limitation of the database and/or data is intended, then clarification of the limitation intended is requested.

Claims 1 and 46 recite that database entities are designed “to mimic” biological entities, and further recite that a first relationship is one “mimicking” a second relationship. It is unclear what is intended by the terms “mimic” and “mimicking” in the context of the claims. The term “mimic” is not defined by the instant specification, and

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Merriam-Webster (online) defined “mimic” as “to imitate closely” or “to simulate.” A database is generally regarded by those skilled in the art of bioinformatics as a compilation of data, not a model or simulation. While “dynamic” databases are known in the art (i.e. those which can be altered upon specific interactions with a user), neither the claims nor specification disclose such a “dynamic” database. It is unclear what limitation of the database (or database entities) is intended by the limitation that the entities “mimic” a biological entity. A database of nucleic acid sequences, for example, REPRESENTS the nucleic acids, but does not comprise simulation or model of the actual polynucleotides. A database comprising 3D coordinates of proteins can be used to model or “mimic” the conformation of the proteins, but generally the database itself is not considered to be one wherein the coordinates “mimic” the conformation of the physical protein. A flux balance analysis (FBA) model simulates relationships among “entities” comprised therein; i.e. the metabolites, etc. used to generate the FBA model. An FBA model, however, is not a database. A database of known metabolites may be used to GENERATE the model, and the database may comprise information with regard to interactions between different metabolites (e.g. as equations), but the database itself does not “mimic” the actual relationships; FBA model is required for “mimicking” the relationships between different metabolites. As it is unclear what limitation of the database and/or entities is intended by the “mimic” and “mimicking” terms, the claims are indefinite.

Claims 1 and 46 recite limitations with regard to “entities” and “macromolecules.” It is not clear what relationship, if any, is intended between the “entities” and

“macromolecules” and any other limitations of the claims. In particular, it is unclear whether the entities and/or macromolecules have any relationship with the expression levels of genes recited in the first step of each claim, or with the genes for which the expression level are obtained, or with the biological characteristics which are selected. AS the relationship between the entities and macromolecules of the database to anything else recited in the claims is unclear, the claims are indefinite.

Claim 1 recites performing one or more statistical methods “to the grouped expression levels,” which is nonsensical. One may calculate statistical methods WITH data such as grouped expression levels, or may APPLY statistical methods/procedures to data, or may perform a number of mathematical manipulation ON data, but those skilled in the art do not perform methods, statistical or otherwise, TO data such as expression levels. As the intended step is unclear, the claim is indefinite.

Claim 46 recites a last step of “clustering,” but fails to recite what is to be clustered. As it is unclear what is to be “clustered” in the final step, the claim is indefinite.

Claims 7, 13-15 and 47-51 depend from claim 1 or 46 and are therefore also indefinite for the reasons set forth above.

Claims 7 and 49 limit the plurality of biological characteristic to “comprise orthologous genes.” It is unclear whether applicant intends to substitute the list of biological characteristics recited in each of claims 1 and 46 for orthologous genes, or whether applicant intends the biological characteristics to FURTHER comprise orthologous genes, therefore the claims are indefinite.



Claim 15 recites that biological characteristics “are retrieved” using SQL statements. It is unclear whether applicant intends an actual method step (i.e. retrieving characteristics) or intends a limitation of the characteristics, or intends some other limitation of the method regarding SQL statements, therefore the claim is indefinite. If a method step is intended, then it is further unclear wherein the method of claim 1 the step is intended to occur. If applicant intends a method step, then the step should be recited using active, positive language.

Claim 47 recites the limitation “the clustering process” in line 1. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite.

Claim 47 recites the limitation “the selected biological characteristics” in line 2. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite. Parent claims 46 recited selecting “at least one biological characteristic,” but does not recite “biological characteristics.”

Claim 48 limits the method of claim 47 to further comprise data mining. It is unclear where in the method of parent claim 46 the data mining is to occur, and what relationship this step is intended to have to any other claim step(s). Further, it is unclear what “data” is to be mined. As the limitations and relationship between steps is unclear, claim 48 is indefinite.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 13-15, 46 and 50-51 are rejected under 35 103(a) as being unpatentable over ZHENG et al. (US 6,263,287) in view of The Gene Ontology Consortium; hereinafter GOC (Nature Genetics (May, 2000) Volume 25, pages 25-29).

ZHENG teaches a method for manipulation and analysis of gene expression data wherein gene expression data is received/provided, and the data is clustered with regard to at least one biological characteristic, which may include tissue origin or genomic information about the gene (abstract and col. 2, lines 18-52), as in claims 1 and 46. ZHENG further teaches that his clustering algorithm can identify functionally related genes with different times curves, wherein the time-curve representation is both literal and numerical (col. 1, lines 54-61), therefore ZHENG's database necessarily includes expression levels and time elements related to the expression levels of genes. An expression level is a representation (mimic) of the amount of gene expressed, and a numerical time of expression "mimics" the relationship between nucleic acids and proteins expressed in cells (i.e. a relationship between "biological macromolecules"), thus ZHENG's database meets the "mimicking" limitations of claims 1 and 46. ZHENG teaches use of SQL (col. 1, lines 61-63), as in claim 15. ZHENG teaches use of data

from Genbank and other databases (col. 10) as in claims 13-14 and 50-51. ZHENG does not teach biological characteristics described using a gene ontology system.

GOC teaches a gene ontology system for describing biological characteristics for a variety of organisms (p. 25) and teaches that this ontology system may be used in analysis and annotation of gene expression data (p. 28). GOC also teaches that ontology is a vital tool enabling researchers to turn data into knowledge (p. 27).

It would have been obvious to one of ordinary skill in the art at the time of invention to have described the biological characteristics in the method of ZHENG using the ontology system of the GOC where the motivation would have been to improve the method using a tool which allows a flexible and dynamic way of comparing homologous gene sequences using a common vocabulary, as taught by GOC (p. 28).

Claims 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over ZHENG et al. (US 6,263,287) and The Gene Ontology Consortium; hereinafter GOC (Nature Genetics (May, 2000) Volume 25, pages 25-29) as applied to claims 46 and 50-51 above, in view of ROCKE et al. (US 2002/0111742).

ZHENG and the GOC make obvious a method for analyzing gene expression data, as set forth above. ZHENG teaches further analysis (mining) of the clustered data (col. 12, lines 40-45 and col. 15, lines 15-67) and the GOC further teaches hierarchical clustering (Fig. 2), but ZHENG and the GOC do not specifically teach multiple dimension clustering.

ROCKE teaches classifying high dimensional data in methods of gene expression analysis (abstract and paragraph 85).

It would have been obvious to one of skill in the art at the time of invention to have performed the dimension reduction of ROCKE on large gene expression databases before clustering in the method of ZHENG and GOC where the motivation would have been to facilitate clustering and permit accurate "classification" of the data, as taught by ROCKE (paragraphs 7 and 17). One skilled in the art would reasonably have expected success in combining ROCKE's dimension reduction with ZHENG and GOC's clustering because all teach analyzing large amounts of gene expression data in order to correlate differential gene expression with tissue or functional specificity (see ZHENG, col. 15, GOC, Fig. 2, and ROCKE, paragraphs 85-86).

Claims 1, 7, 13-15, 46, and 49-51 are rejected under 35 U.S.C. 103(a) as obvious over GARNER et al. (US 2003/0033290) and OGATA et al. (Nucleic acids Res. (1999) vol. 27, no. 1, pp. 29-34) in view of The Gene Ontology Consortium; hereinafter GOC (Nature Genetics (May, 2000) Volume 25, pages 25-29).

GARNER teaches a method for analysis of genetic databases (abstract) wherein gene expression data is obtained and clustered according to selected biological characteristics, including genomic information and biological function (paragraphs 8, 82 and 151-152). As genomic information is related to biological function, the data of GARNER necessarily "mimics" both biological entities (genes) and relationships between macromolecules (biological functions), as in claims 1 and 46. GARNER

teaches a variety of databases (paragraph 158), including KEGG, and use of SQL software (paragraph 150), as in claims 13-15 and 50-51.

OGATA provides support that KEGG comprises information with regard to orthologous genes (p. 33, left column), therefore GARNER's teaching of KEGG is inherently a teaching for biological information comprising orthologous genes, as in claims 7 and 49.

Neither GARNER nor OGATA teach biological characteristics described using a gene ontology system.

GOC teaches a gene ontology system for describing biological characteristics for a variety of organisms (p. 25) and teaches that this ontology system may be used in analysis and annotation of gene expression data (p. 28). GOC also teaches that ontology is a vital tool enabling researchers to turn data into knowledge (p. 27).

It would have been obvious to one of ordinary skill in the art at the time of invention to have described the biological characteristics in the method of GARNER and OGATA using the ontology system of the GOC where the motivation would have been to improve the method using a tool which allows a flexible and dynamic way of comparing homologous gene sequences using a common vocabulary, as taught by GOC (p. 28).

Applicant's arguments filed 8/11/06 have been fully considered but they are not persuasive. In response to the argument that ZHENG, ROCKE, GARNER and OGATA, even if combined, do not teach or suggest a database "including entities being designed

to mimic biological entities, a first relationship among biological entities mimicking a second relationship among biological macromolecules,” it is noted that both ZHENG and ROCKE do teach use of data comprising gene expression information and information with regard to “relationships” between macromolecules, and thus inherently teach databases “mimicking” biological entities (genes and/or proteins) wherein temporal expression and biological function information “mimics” relationships among macromolecules, as set forth above. In response to the argument that none of the references, alone or combined, teach or suggest grouping expression levels according to a selected biological characteristic or “performing one or more statistical methods to the grouped expression levels,” it is noted that both ROCKE and ZHENG teach clustering according to selected biological characteristics, and the GOC teaches hierarchical clustering. As clustering is a form of “grouping” and requires at least some statistical analysis, the examiner maintains that each of ZHENG, ROCKE and the GOC, at least teach grouping and statistical analysis. Applicant has not presented any reasons, other than the conclusory one reflected above, for why the clustering explicitly taught by ZHENG, ROCKE, and the GOC (previously set forth and reiterated above) should not be considered a type of “grouping.” For these reasons and those set forth above, the rejection of claims 1, 7, 13-15 is maintained and claims 46-51 are rejected.

### ***Conclusion***

Claims 1, 7, 13-15 and 46-51 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Monday-Friday; 6 am-2:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631

*Marjorie A. Moran*  
10/25/06